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U.S. NATIONAL CANCER INSTITUTE  
GUIDE TO THE LABORATORIES

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A GUIDE

TO

THE

LABORATORIES

of the  
U.S. NATIONAL  
CANCER  
INSTITUTE



FEDERAL SECURITY AGENCY — PUBLIC HEALTH SERVICE

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## CANCER CONTROL

Room 120 - The Cytologic Test for Cancer. Miss Evelyn Thompson

The Cytologic Test consists of microscopic examination for abnormal cells in a specially prepared smear of body secretion--vaginal, bronchial, gastric, urine sediment, rectal, prostatic. The smear is fixed in alcohol-ether, and the polychrome stain developed by Papanicolaou is applied. Specially trained workers can then identify cells exfoliated from precancerous and cancerous lesions, and may thereby aid in diagnosis, possibly before the development of symptoms. The test is particularly effective in screening examinations for cancer of the female genitalia. Cancer of the cervix uteri is indicated by the appearance of cells that show much variation in form and size, atypical nuclei, and vacuolization of the cytoplasm.

## BIOLOGY

Room 115 - Mice of Inbred Strains Used in Cancer Research. Dr. H. B. Andervont

Strain dba. Established by C. C. Little in 1909. Oldest inbred strain; over 100 generations. Medium incidence of leukemia, and breeding females have high incidence of mammary tumors.

Strain A. Established by L. C. Strong. Inbred for 75 generations. High incidence of lung tumors, and breeding females have high incidence of mammary tumors.

Strain C3H. Established by L. C. Strong. Inbred for about 70 generations. High incidence of mammary tumors, and moderate incidence of hepatomas.

Strain CBA. Established by L. C. Strong. Inbred for 67 generations. Medium incidence of mammary tumors.

Strain C. Established by E. C. MacDowell. Inbred for 64 generations. Medium incidence of pulmonary tumors. Genetically susceptible to the mammary tumor agent.

Strain I. Established by L. C. Strong. Inbred for 50 generations. Susceptible to adenomatous hyperplastic lesions of the stomach.

Strain C58. Established by E. C. MacDowell. Inbred for about 80 generations. High incidence of leukemia.

Strain C57 Black. Established by C. C. Little. Inbred for about 75 generations. Low incidence of mammary and pulmonary tumors.

Strain L. Established by J. M. Murrey from a mutation of C57 Brown. Inbred for about 65 generations. Low incidence of mammary and lung tumors, and medium incidence of a lesion resembling Hodgkin's disease.

## BUILDING 6

### First Floor

Room 105 - Studies in Cell Survival and Adaptation, Using Paramecia and Bacteria. Dr. R. R. Spencer and Mr. Malcolm Melroy

Processes similar to some that occur in cancer have been observed in this laboratory when bacteria and protozoa were exposed to carcinogens over many generations. Strains of paramecia, long exposed to methylcholanthrene and then removed, showed enhanced survival value and population levels. Moreover, certain species tended to adapt to unnatural conditions when exposure was rhythmic, but perished when continuous. The possible bearing of these adjustment processes on the genesis of mammalian cancer is being investigated.

### BIOCHEMISTRY

Room 109 - Studies in Metabolism and Diagnosis of Neoplasms. Dr. Dean Burk

Malignant tumors, as a class of tissue, have a fairly characteristic metabolism. The end products of metabolism may be delicately and accurately measured with manometric, polarographic and spectroscopic instruments. The manometer measures very small amounts of gas exchange; the polarograph, small amounts of dissolved liquids or solids; and the spectroscope, small amounts of light at different wave lengths. Blood sera or plasma of tumor-bearing animals, and thin slices of tumor tissue, provide excellent materials for study. Of special interest in these investigations are the mitochondria and other sub-cellular particulates, derangements of which may be closely connected with the cause or maintenance of malignancy.

### Second Floor

Room 213 - Biochemistry Laboratories. Dr. J. P. Greenstein

Morphologic and physiologic differences between normal and cancerous tissues suggest chemical differences, which indicate approaches to therapy. Projects include comparative metabolism and enzyme studies; comparison of proteins, fats and other tissue components common to the normal and malignant states; and studies of intermediary metabolism and nutrition, employing isotopes as tracers. Some of the equipment used will be shown in the sub-basement of Building 6.

BUILDING 6

Second Floor

Hall - Enzyme Patterns in Tumors and Normal Tissues.

The enzyme patterns of normal tissues are highly differentiated, and vary markedly from one tissue to another. In tumors, however, the patterns tend toward undifferentiation. Regardless of the etiology or histogenesis of the tumors, their enzyme patterns tend to be nearly uniform, and to resemble those of embryonic tissue.

Room 218 - Physicochemical Laboratory: Stable Isotopes as Tracers in Tumor Metabolism. Dr. Julius White

This laboratory is engaged in metabolism studies to determine the fate of amino acids and carcinogenic agents in normal and tumor-bearing animals. In the synthesis of compounds to be traced, elements ordinarily present are replaced by isotopes. These are later retrieved from the organs and measured. The synthesis of amino acids and carcinogens, with substitution of a stable isotope of nitrogen, will be illustrated, and apparatus for retrieving the isotopes will be shown.

Room 209 - Effects of Thiouracil on C3H Mice. Dr. H. P. Morris, Miss Celia Dubnik, and Dr. A. J. Dalton

In C3H mice, prolonged ingestion of extremely large amounts of a goitrogenic compound, thiouracil, may upset the hormonal balance, and will eventually result in a greatly reduced mammary tumor incidence and in thyroid metastasis to the lungs. The experimental results and an explanation of the possible mechanism will be given.

Room 205 - Studies on Proteinase Activity in Normal and Neoplastic Tissues. Dr. Mary Maver

In the study of neoplasia, the proteinases of animal tissue, or cathepsins, are of particular interest, since they probably serve as catalysts in the synthesis of protein. These intracellular enzymes differ from the proteinases of the digestive tract in their pH optima and their activation of reducing substances.

Room 233 - Methods for Isolation and Characterization of Proteins from Malignant and Normal Tissues. Dr. Joseph Shack

This laboratory is engaged in the separation, purification and characterization of proteins of malignant tissues, and in the comparison of these proteins with those of normal tissues. Procedures in the low-temperature alcohol fractionation method will be shown.

BUILDING 6

Third Floor

ENDOCRINOLOGY

Room 301 - Demonstration of Growth-Promoting Effects of Vitamins and Hormones. Dr. Roy Hertz

Rapid and massive tissue growth may be induced in various organs of the body by means of the steroid and pituitary hormones. These hormones do not act independently, but depend in large measure on vitamins and other nutritional factors for their effect. The exhibits will include hormone-stimulated tissue from animals on various diets.

Room 303 - Microbiologic Methods for Assaying Vitamins and Amino Acids. Mr. F. C. Dhyse

Certain vitamins and amino acids required for the growth of mammalian organisms are also needed by some bacteria. The growth of these bacteria in response to nutritional factors can be used as a measure of the amount of various vitamins and amino acids present in normal and abnormal tissues of the body. The methods employed for such assays, and some of their applications, will be demonstrated.

Room 305 - Chemical Method for Assaying Ketosteroid and Gonadotropic Hormone Extractions. Dr. B. B. Westfall

Metabolic studies of patients with cancer and with hormone-producing tumors of various types are conducted with the aid of such determinations as the urinary secretion of 17 ketosteroids, estrogens, and gonadotropic hormones. The biochemical methods used in these investigations will be demonstrated, and some of the clinical cases that have been studied will be discussed.

BIOLOGY

Room 310 - Transparent Chamber Technique for Study of Tumor Histophysiology in the Live Mouse. Dr. Glenn Algire

The transparent chamber attached to the animal permits in vivo microscopic observation of the growth and vascular development of tissues, neoplastic and normal, over periods exceeding 100 days. Using oil-immersion objectives, examination and photography are performed at magnifications up to 1000X. The method is employed to study cell migration and division, effects of chemical and physical agents on tumors, problems of tumor induction and growth, and circulatory physiology.

BUILDING 6

Third Floor

Room 313 - A Permanent Gastric Fistula for Long-Term Investigations in the Dog. Dr. Morris Barrett

The fistula is constructed from an isolated, short segment of jejunum. The segment, with intact blood and nerve supply, is resected, and the continuity of the intestine is re-established by end-to-end anastomosis. The isolated segment is so rotated that peristalsis is toward the stomach. An oblique-to-side anastomosis is made on the anterior surface of the stomach, about midway between the greater and lesser curvature, and the proximal end of the jejunal segment is then brought out through a muscle-splitting incision.

Such fistulas have been maintained in the dog for as long as seven years, without apparent effect upon general health or gastric physiology. No ulcers have been observed. Without further alteration, the stomach is made easily accessible for endoscopic examination, gastric analysis, or the introduction of materials used in experimental procedures.

Room 322 - Technique for Quantitative Morphologic Analysis of Tissue. Dr. H. W. Chalkley

This technique, developed at the National Cancer Institute, provides an accurate estimate of the proportion of tissue components, one to another, that may be clearly differentiated under the microscope. A tissue section is so placed in the field that one of five pointers fixed in the eyepiece "touches" a certain component, such as a cell nucleus. The nuclei "hit" by the other four pointers are counted. This procedure is repeated many times, and a cumulative average of hits is made. From this the proportion of nuclear to cytoplasmic material is determined. The technique is being used at several institutions, including the Carnegie Institute, where studies have been undertaken to correlate chemical and morphologic changes during development of the chick embryo.

Rooms 323-333 - Tissue Culture Unit. Dr. W. R. Earle

During the past eight years, the tissue culture unit has been concerned with effecting the transformation of normal to malignant cells *in vitro*. (See Jour. of the Nat. Cancer Inst., Oct. 1943 and later.) Present activities, for the most part, are directed toward increasing the accuracy and applicability of procedures for the cultivation of tissue, with particular reference to cancer research.

To this end, a technique has been worked out for growing the cells under a sheet of perforated cellophane, which obviates the

BUILDING 6

Third Floor

need for the plasma clot. This advance has afforded much larger cultures than were previously possible. One of the cultures on exhibit contains, at the end of 38 days' growth, approximately 0.1 gm. of tissue.

Another accomplishment of the laboratory is the working out of a procedure that has allowed, for the first time, the growth of an isolated sarcoma cell in vitro. These advances will make possible the growth of extremely large cultures from a single cell.

- (a) 323 - Sterilizer room, with egg incubator for providing chick embryos.
- (b) 330 - Sterile room for planting and transfer of tissue cultures.
- (c) Hall - Transformation of normal to malignant tissue in vitro.
- (d) 333 - Special incubators for tissue culture; microscope units (incubated) for examination of tissue; camera for photo-micrography at 37.5 C.
- (e) 333 - Tissue culture grown under perforated cellophane sheet.
- (f) 333 - Culture grown from isolated sarcoma cell.

Attic

Room 416 - Studies on Differentiation, Growth, and Regeneration, Using the Fish as an Experimental Animal. Dr. Clifford Grobstein

Basement

Room B9 -- Relation of Viruses to the Cancer Problem, with Emphasis on Bioassay of a Chicken Tumor Virus. Dr. Ray Bryan

**BIOPHYSICS**

Room B14 - Counter Equipment for Measurement of Radioactive Material.

Room B28 - X-Ray Equipment and Techniques for Irradiation Studies of Animals.

This X-ray equipment (200 K.V.) was designed and constructed at the National Cancer Institute for irradiation studies of animals.

## BUILDING 6

### Basement

The dual-tube design eliminates rectifier tubes and doubles the capacity. To minimize danger to the operator, the control panel is outside a lead-lined room containing the machine, which may be viewed through a lead-glass window during operation. Techniques for part- and whole-body irradiation will be shown.

### Sub-Basement

#### Room SB6 - Ultracentrifuge.

The ultracentrifuge consists of a metal rotor, which spins at high speed in a vacuum chamber, and a driving mechanism, usually a small turbine driven by high-pressure air jets.

For concentrating dissolved particles, the solution is put in tubes, which are fitted into the rotor. After spinning for a suitable time, the particles collect on the bottoms of the tubes.

For analytical study, the rotor is equipped with a transparent cell in which the solution is placed, and the chamber is equipped with heavy glass windows. A beam of light is projected through the system so that it passes through the rotating cell. By photographing the beam of light at successive time intervals, the motion of heavy particles in the solution can be followed, and from this, information about the rate of sedimentation and, in some cases, about the size of the particles can be obtained.

#### Room SB8 - Electron Microscope and Photomicrographs of Cellular Particles.

The electron microscope is about 100 times as powerful as the ordinary microscope. The objects it reveals are measured in millimicrons.

With the ordinary microscope, objects shorter than 0.27 micron are invisible, since the magnifying power is limited by the wave length of visible light. Ultraviolet light, which has a shorter wave length, extends the limit to approximately 0.12 micron. This, however, is grossly inadequate for the observation of most viruses.

Instead of light, the electron microscope uses particles of electricity from the cathode of a vacuum tube--electrons. The "lenses" of this instrument are coils of wire carrying an electric current that creates a magnetic field, which makes the beam of electrons converge as a glass lens does light rays. The image is received on a fluorescent screen or photographic plate.

Photomicrographs of cellular particles revealed by the electron microscope will be exhibited.

BUILDING 6

Sub-Basement

Room SB9 - High-Speed Microtome.

This machine consists, essentially, of a high-velocity rotating knife, arranged with a slow-velocity feed for the material to be sliced. It cuts extremely thin slices of tissue, which can be studied under the electron microscope.

Room SB11 - Electrophoretic Equipment.

This equipment is used for separating the proteins in a solution such as blood serum. An electric current is passed through the serum, and the various proteins move at different velocities through the electrophoretic cell. The pattern of protein velocities can be photographically registered. This gives information about the condition of the blood from which the serum was derived.

Room SB12 - Mass Spectrometer.

This instrument is used in cancer research to analyze compounds containing heavy isotopes, in order to trace the course of elements through the animal body. Samples of organs, tissues or excreta are taken at various times, and the isotopes therein are converted to gas, which the mass spectrometer measures.

To do this, the instrument bombards the molecules of the gas with electrons, accelerates with an electrical field the ions thus formed, and curves the paths of the ions with an electromagnet. For a given magnetic field and ion velocity, the radius of curvature of the ion path is proportional to the mass of the ion and inversely proportional to its charge. The charges of the sorted ions are collected and amplified at the ends of the paths, and measured to determine the relative abundance of the molecules of each mass.

BUILDING 8

Ground Floor

BIOLOGY

Room 4 - Investigations of Hereditary Influence on the Development of Tumors in Mice. Dr. W. E. Heston

Through inbreeding with selection over many years, geneticists have developed strains of mice with high incidences of spontaneous tumors--mammary, lung, liver, etc.--and other strains in which these tumors are infrequent. Crossing of strains has shown that types of tumor can be linked with coat color and developmental genes. In addition, crossing has revealed the effects of extra-chromosomal factors, such as the mammary tumor milk agent.

Inbred strains of rats and guinea pigs have also been produced for cancer research purposes.

Room 6 - Experimental Studies of Leukemia. Dr. Lloyd Law

The demonstration will comprise (1) mice of inbred leukemic strains--C58, RIL, Se se-C and NB; (2) transplantable leukemias--spontaneous, X-ray- and carcinogen-induced; and (3) typical pathology of leukemias in mice.

Room 8 - Studies on Mammary Tumors in the Mouse. Dr. Bertrand Bennison

Room 21 - Maintenance and Breeding of Mice for Experimentation. Mr. J. H. Miller

First Floor

CHEMOTHERAPY

Rooms 100-122 - Chemotherapy Laboratories. Dr. M. J. Shear

In general the work of these laboratories is directed toward preparation and investigation of chemical agents that may lead to a chemical treatment of cancer in man. At present most chemicals that are effectively tumor-necrotizing are unduly toxic. Some degree of progress with respect to mouse tumors, however, has been reported, with certain agents such as bacterial metabolites, organic arsenical compounds, colchicine derivatives and podophyllin. Since these investigations are directed ultimately toward treatment of patients, more extensive collaboration with clinicians is projected as the experimental work advances.

BUILDING 8

First Floor

- (a) 112 - General plan of approach to experimental cancer chemotherapy. Dr. M. J. Shear
- (b) 101, 103, 108 - Organic chemistry (synthesis, preparation, constitution) of agents for the chemotherapy program. Drs. J. L. Hartwell, J. M. Johnson, and D. L. Vivian
- (c) 118 - Solubility and toxicity determinations of selected chemical agents in normal animals. Preparation and testing of bacterial metabolites for tumor-necrotizing potency. Mr. Adrian Perrault
- (d) 120 - Transplantation of tumors for screening procedures. Miss Faith Jouvenal
- (e) 116 - Procedures for screening of chemical agents against animal tumors. Mr. Joseph Leiter
- (f) 216 (Second floor) - Cytologic criteria for evaluating effects of chemical agents on animal tumor cells. Dr. R. C. MacCardle
- (g) 115, 117 - Pharmacologic action of drugs and chemical agents found to affect tumors. Drs. Morris Belkin and L. B. Dennis
- (h) 100 - Physiologic responses of animals to administration of tumor-necrotizing agents. Dr. L. V. Beck
- (i) 106 - Immunologic and cellular responses following administration of tumor-necrotizing agents to tumor-bearing animals. Dr. Horace Goldie
- (j) 104 - Regression experiments in animals, and implications for clinical work. Dr. E. Greenspan
- (k) 212 (Second Floor) - Clinical aspects of the chemotherapy program. Dr. Virginia Downing

Second Floor

Room 216 - See (f) above.

Room 212 - See (k) above.

BUILDING 8

Second Floor

PATHOLOGY

Room 220A - Experimental Gastro-Intestinal Cancer. Dr. H. L. Stewart

Cancers of the stomach and small intestine have been induced by feeding or direct injection of carcinogens. Sites of action vary with the means of administration. The histogenesis of gastro-intestinal tumors in mice will be illustrated with photographs of the gross and microscopic lesions.

Room 221A - Experimental Studies on Tumors of the Testis. Dr. H. I. Firminger

Progress in the study of testicular tumors has been delayed by the inadequacy of methods for inducing them in experimental animals. It has been found, however, that interstitial cell tumors of the mouse testis can be induced with estrogens. This exhibit includes photomicrographs of testicular tumors that developed in strain C mice after subcutaneous implantation of 5 to 100 per cent stilbestrol pellets. Various stages of development from hyperplasia and pigmentation to nodule formation and metastasis are illustrated.

Room 221 - Melanin Formation Resulting from Treatment of Mouse Skin with Chemical Carcinogen. Dr. F. H. Burgoyne

Application of 5,9,10-trimethyl-1,2-benzanthracene to the skin of experimental animals induces cutaneous and subcutaneous tumors. The period required for this change is approximately 7 to 11 months. In association with these neoplasia, local areas of pigment accumulation appear. This suggests that production of pigment is causally related to stimulation by the carcinogenic agent.

Room 218 - Normal and Pathologic Anatomy of Mouse Kidneys. Dr. Thelma Dunn

Room 219 - Histogenesis of Pulmonary Tumors in Mice Following Administration of Urethane. Drs. F. K. Mostofi and C. D. Larson

The earliest morphologic changes preceding and accompanying the development of pulmonary tumors induced by oral administration of urethane have been studied in mice. Opinion differs as to



BUILDING 8

Second Floor

whether these tumors originate in the bronchial epithelium or alveolar cells, and whether they are preceded by such conditions as inflammation or atelectasis. The photomicrographs on exhibit indicate that these tumors originate in cells of the alveolar lining, and are not preceded by atelectasis, inflammation, or bronchial changes.

Room 217 - Estrogen-Induced Fibroid Tumors in Guinea Pigs.

Dr. E. M. Nadel

This exhibit includes photomicrographs of tumors that arose in the uterus and peritoneum of strain 13 guinea pigs after stimulation for three months by subcutaneously implanted fusion pellets of 50 per cent stilbestrol in cholesterol. The relation of nutrition to the development of these tumors is being studied.

Room 210 - Experimental Cancer of the Liver. Dr. A. S. Mulay

Room 208 - Progesterone-Induced Mammary Tumors in Pregnant Mice.

Dr. Alexandre Symeonidis

Room 208 - Survival of Mammary Cancer Cells of Mice, in Vitro and in Heterologous Hosts. Dr. I. V. Li

Rooms 200, - Histopathology and Photomicrography. Mr. A. M. Kessel  
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The preparation of tissues from experimental animals is an important function of the Pathology Section. Methods for the fixation, embedding, and routine and special staining of tissues will be demonstrated, and several labor-saving devices displayed. Museum preparation of whole animals and organs, and photographic methods for recording unusual lesions, will be shown.









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